

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
7 December 2000 (07.12.2000)

PCT

(10) International Publication Number
WO 00/73330 A3

(51) International Patent Classification⁷: G01N 33/50, (81) Designated States (national): AE, AG, AL, AM, AT, AU, 33/68, C07K 14/47 AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(21) International Application Number: PCT/GB00/02110

(22) International Filing Date: 1 June 2000 (01.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9912741.7 1 June 1999 (01.06.1999) GB
0002973.6 9 February 2000 (09.02.2000) GB

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(72) Inventors; and

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(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— With international search report.
— Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

(88) Date of publication of the international search report:
22 February 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/73330 A3

(54) Title: METHOD AND COMPOSITIONS RELATING TO INSULIN RESISTANCE DISORDERS

(57) Abstract: Methods and compositions relating to insulin resistance are disclosed. Specifically, proteins that are differentially expressed in these conditions are identified. In one aspect, the invention provides a method of screening an agent to determine its usefulness in treating insulin resistance, based on establishing a paradigm in which at least one protein is differentially expressed in relevant tissue from, or representative of, subjects having differential levels of insulin sensitivity.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02110

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 G01N33/50 G01N33/68 C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 46404 A (DAS RINA ; JETT MARTI (US); MENDIS CHANAKA (US); WRAIR WALTER REED) 10 August 2000 (2000-08-10) Claims page 17, last paragraph -page 18, paragraph 1 ---	1-27, 29-32, 34-42, 44
E	WO 00 32779 A (LEPTIN MARIA) 8 June 2000 (2000-06-08) page 5, line 7 - line 13 page 48, line 31 -page 49, line 11 ---	1-27, 29-32, 34-42, 44
E	WO 00 32618 A (EXELIXIS PHARMACEUTICALS INC) 8 June 2000 (2000-06-08) page 50, line 31 -page 51, line 5 --- -/-	1-27, 29-32, 34-42, 44

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

15 November 2000

Date of mailing of the international search report

28/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Routledge, B

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/02110

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>LEE S C ET AL: "Proteome analysis of rat skeletal muscle: Characterization of a novel form of insulin resistance associated protein p20." FASEB JOURNAL, vol. 11, no. 9, 1997, page A949 XP002151830</p> <p>17th International Congress of Biochemistry and Molecular Biology in conjunction with the Annual Meeting of the American Society for Biochemistry and Molecular Biology; San Francisco, California, USA; August 24-29, 1997</p> <p>ISSN: 0892-6638</p> <p>the whole document</p> <p>---</p>	1
X	<p>EDVARDSSON ULRIKA ET AL: "A proteome analysis of livers from obese (ob/ob) mice treated with the peroxisome proliferator WY14,643." ELECTROPHORESIS, vol. 20, no. 4-5, April 1999 (1999-04), pages 935-942, XP000964564</p> <p>ISSN: 0173-0835</p> <p>the whole document</p> <p>---</p>	1-27, 29-32, 34-42, 44
A	<p>US 5 795 726 A (GLUCKSMANN M ALEXANDRA) 18 August 1998 (1998-08-18)</p> <p>column 10, line 13 - line 40</p> <p>---</p>	1-27, 29-32, 34-42, 44

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/02110

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 0046404	A 10-08-2000	NONE			
WO 0032779	A 08-06-2000	US	6135942 A	24-10-2000	
		AU	1968800 A	19-06-2000	
WO 0032618	A 08-06-2000	AU	1748400 A	19-06-2000	
US 5795726	A 18-08-1998	US	5800998 A	01-09-1998	
		AU	5252698 A	03-06-1998	
		WO	9821239 A	22-05-1998	

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box I.2

Claims Nos.: 28,33,43,45-52

Present claims 28, 33, 43 and 52 lack support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT with regard to essential technical features for the embodiments claimed, thus rendering a meaningful search over the whole of the claimed scope is impossible.

Present claims 45-51 relate to an extremely large number of possible proteins. In fact, the claims contain so many possible proteins and variables (e.g. use of "...may..." claims 46-49) that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Indeed it is acknowledged that at least some of the claimed proteins e.g. LOMT19 are known (HSP60) in the prior art thus indicating that the claims do not determine the subject matter for which protection is sought.rendering the subject matter.

The search was limited to the use of differential protein expression in the detection and monitoring of insulin resistance.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

Date of mailing (day/month/year) 21 February 2001 (21.02.01)	ETATS-UNIS D'AMERIQUE in its capacity as elected Office
International application No. PCT/GB00/02110	Applicant's or agent's file reference SJK/BP5859228
International filing date (day/month/year) 01 June 2000 (01.06.00)	Priority date (day/month/year) 01 June 1999 (01.06.99)
Applicant CAWTHORNE, Michael et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

27 December 2000 (27.12.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer S. Mafla</p> <p>Telephone No.: (41-22) 338.83.38</p>
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PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

KIDDLE, Simon, J.
 Mewburn Ellis
 York House
 23 Kingsway
 London WC2B 6HP
 ROYAUME-UNI

15 DEC 2000

Date of mailing (day/month/year) 07 December 2000 (07.12.00)	
Applicant's or agent's file reference SJK/BP5859228	
International application No. PCT/GB00/02110	International filing date (day/month/year) 01 June 2000 (01.06.00)
Priority date (day/month/year) 01 June 1999 (01.06.99)	
Applicant PROTEOME SCIENCES PLC et al	

IMPORTANT NOTICE

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the International application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AG,AU,DZ,KP,KR,MZ,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW
 The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the International application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 07 December 2000 (07.12.00) under No. WO 00/73330

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference SJK/BP5859228	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)																
International application No. PCT/GB00/02110	International filing date (day/month/year) 01/06/2000	Priority date (day/month/year) 01/06/1999																
International Patent Classification (IPC) or national classification and IPC G01N33/50																		
<p>Applicant PROTEOME SCIENCES PLC</p> <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>																		
<p>3. This report contains indications relating to the following items:</p> <table> <tr> <td>I</td> <td><input checked="" type="checkbox"/> Basis of the report</td> </tr> <tr> <td>II</td> <td><input type="checkbox"/> Priority</td> </tr> <tr> <td>III</td> <td><input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>IV</td> <td><input type="checkbox"/> Lack of unity of invention</td> </tr> <tr> <td>V</td> <td><input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td>VI</td> <td><input type="checkbox"/> Certain documents cited</td> </tr> <tr> <td>VII</td> <td><input type="checkbox"/> Certain defects in the international application</td> </tr> <tr> <td>VIII</td> <td><input checked="" type="checkbox"/> Certain observations on the international application</td> </tr> </table>			I	<input checked="" type="checkbox"/> Basis of the report	II	<input type="checkbox"/> Priority	III	<input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	IV	<input type="checkbox"/> Lack of unity of invention	V	<input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	VI	<input type="checkbox"/> Certain documents cited	VII	<input type="checkbox"/> Certain defects in the international application	VIII	<input checked="" type="checkbox"/> Certain observations on the international application
I	<input checked="" type="checkbox"/> Basis of the report																	
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VI	<input type="checkbox"/> Certain documents cited																	
VII	<input type="checkbox"/> Certain defects in the international application																	
VIII	<input checked="" type="checkbox"/> Certain observations on the international application																	

Date of submission of the demand 27/12/2000	Date of completion of this report 28.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Wieser, M Telephone No. +49 89 2399 8434



INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/GB00/02110

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-110 as originally filed

Claims, No.:

1-52 as originally filed

Drawings, sheets:

1/66-66/66 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/02110

the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.

claims Nos. 28,29,33-38,43,45-52.

because:

the said international application, or the said claims Nos. 38, industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 29,34-38 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. 28,33,43,45-52.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.

the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 3,5,6,8-14,16,17,19-24,29-31,39-42,44

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/02110

No: Claims 1,2,4,7,15,18,25-27,32

Inventive step (IS) Yes: Claims

No: Claims 1-27,30-32,39-42,44

Industrial applicability (IA) Yes: Claims 1-27,30-32,39-42,44

No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

S ection III

1. Claims relating to inventions in respect of which no International Search Report has been established need not to be the subject of International Preliminary Examination (Rule 66(1)(e) PCT). Accordingly, claims 28,33,43 and 45-52 are not subject of this written opinion.
2. In addition, the subject-matter of claims 29 and 34-38 is so unclear (Art. 6 PCT), that no opinion on novelty and inventive step can be given. Claim 29 refers to a method according to claims 1-28, wherein the differentially expressed protein (DEP) is a member of a group of proteins which are designated by internal designations only. Said designations are meaningless for a skilled person. In claim 34 the same designations are used to define a protein for use in a method for medical treatment. Claim 35, and dependent claim 36, refer to the use of any agent identified by the method of claims 1-32. A chemical substance cannot be properly defined in a claim by reference to a method for its identification. The same applies to claim 38. In claim 37 the used agents are defined by the above mentioned internal designations.
3. Claim 38 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Section V

4. The following document mentioned in the International Search Report is considered as being the most relevant prior art:
 - (A) ELECTROPHORESIS, vol.20, no.4-5,
April 1999, pages 935-42
5. Document A describes a proteome analyses of livers from obese diabetic (ob/ob) mice treated with the PRAR α agonist WY14,643. Obese ob/ob mice and lean litter mates are treated orally with the agent, then killed and the livers are removed and

snap-frozen. The liver protein compositions are investigated by high-resolution two-dimensional gel electrophoresis. It is shown that WY14,643 produces upregulation of 16 proteins, 14 thereof are found to be components of the peroxisomal fatty acid metabolism. It is concluded that the used animal model of insulin resistance and diabetes points to a therapeutic effect of the tested PRAR α agonist, and subsequent studies with similar agents are envisaged (see abstract, discussion and table 1).

6. The Applicant argues, that document A, contrary to the present application, does not describe the identification of markers linked to insulin resistance and the use of such markers in a method of screening for agents which are capable of changing the expression of these markers. It is the opinion of the authority in charge of the International preliminary Examination, that the 16 proteins found in document A to be upregulated in ob/ob mice after WY14,643 treatment have to be considered as being "markers linked to insulin resistance" as defined by the Applicant. Moreover, the Applicant holds, that document A1 does not describe the comparison between subjects according to the paradigms in the present application. The paradigm as defined in claim 1, saying that at least one protein is differentially expressed in tissue from "subjects having differential levels of insulin sensitivity", is considered as being nothing more than a statement which stands beyond any doubt in professional circles. The "subjects" are defined in more detail in dependent claims 4,5,8,10 and 12 to 17, as being for instance "normal subjects" or as being "abnormally insulin sensitive", "comparatively insulin sensitive", "insulin resistant", having "acquired higher than normal sensitivity", which are either treated with the agent to be tested or not. Using the wording of the claims, document A seems to disclose a method wherein a substance, WY14,643, is tested for its usefulness in treating insulin resistance, by obtaining tissue samples from normal and from insulin resistant subjects which have been treated with the substance, and determining the presence of differentially expressed proteins.

The disclosure in document A is considered to anticipate the novelty of claims 1,2,4,7,15,18,25-27 and 32. These claims do not meet the requirements of Article 33(2) PCT.

7. In the light of the disclosure in document A, the subject-matter of claims 3,5,6,8-14,16,17,19-24,30,31,39-42 and 44, does not seem to be based on an inventive concept *per se*, contrary to the requirements of Article 33(3) PCT.
8. For the assessment of the present claims 38 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claim. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VIII

9. The term "by reference to a previous correlation between such a determination and clinical information" in claim 39 item (d) is not clear and obscures the scope of the claim (Article 6 PCT).
10. Terms like "normal", "abnormal", "comparatively sensitive" and "higher than normal" are open to interpretation and obscure the scope of the claims in which they are used (Article 6 PCT).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SJK/BP5859228	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 02110	International filing date (day/month/year) 01/06/2000	(Earliest) Priority Date (day/month/year) 01/06/1999
Applicant PROTEOME SCIENCES PLC		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

METHOD AND COMPOSITIONS RELATING TO INSULIN RESISTANCE DISORDERS

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 28,33,43,45-52

Present claims 28, 33, 43 and 52 lack support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT with regard to essential technical features for the embodiments claimed, thus rendering a meaningful search over the whole of the claimed scope is impossible.

Present claims 45-51 relate to an extremely large number of possible proteins. In fact, the claims contain so many possible proteins and variables (e.g. use of "...may.." claims 46-49) that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Indeed it is acknowledged that at least some of the claimed proteins e.g. L0MT19 are known (HSP60) in the prior art thus indicating that the claims do not determine the subject matter for which protection is sought.rendering the subject matter.

The search was limited to the use of differential protein expression in the detection and monitoring of insulin resistance.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.